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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/611,598	06/30/2003	Johannes B.M.M. Van Bree		2502

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EXAMINER	
LANKFORD JR, LEON B	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 08/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/611,598	VAN BREE ET AL.	
	Examiner	Art Unit	
	Leon Lankford	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 June 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,36,38,40,41,43,56-58 and 65-67* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,36,38,40,41,43,56-58 and 65-67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's arguments filed 6/1/2006 have been fully considered but they are not persuasive. The claims remain rejected (under 35 USC 103) for the reasons set forth in the previous office action.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicant argues that there must be some degree of predictability for obviousness, and, of course, the examiner concurs. The results demonstrated by applicant are predictable from the teachings and suggestions of the prior art. Given that that prior art is clearly suggestive of using the same enzyme to treat the same disorder, one of ordinary skill in the art would predict that by optimizing the therapeutic protocol you'd get some results.

Generally, differences in concentration or regimen will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or regimen is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the

motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages. For other cases applying this principle, see Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); In re Kulling, 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997).

Applicant's arguments have been considered however a showing to overcome a prima facie case of obviousness must be clear and convincing(In re Lohr et al. 137 USPQ 548) as well as commensurate in scope with the claimed subject matter (In re Lindner 173 USPQ 356; In re Hyson, 172 USPQ 399 and In re Boesch et al., 205 USPQ 215 (CCPA 1980).

Claim Rejections - 35 USC § 112

The rejections under the first paragraph of 35 U.S.C. 112 have been overcome by applicants' amendments and arguments.

Claim Rejections - 35 USC § 102

All of the anticipation rejections have been overcome by applicant's amendments and arguments .

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1,36,38,40,41,43,56-58 and 65-67 are rejected under 35 U.S.C. 103(a) as being unpatentable de Barsy et al (Birth Defects, Original Article Series, Vol. IX, No.2, pages 184-190 (1973)), Williams et al (Birth Defects: Original Article Series, Vol. XVI, No. 1, pages 415-423 (1980)) and Reuser et al (U.S. Pat. 6,118,045), in view of Bijvoet et al (Biochim. Biophys. Acta 1308:93-96 (1996)) and Van Hove et al (Biochem. Mol. Biol Int'l. 43(3):613-623 (1997)).

The claims recite the treatment of infantile

Pompe's disease wherein at least 10 mg/kg body weight per week of human acid α-glucosidase are administered to a patient which survives at least to one year of age. Each of de Barsy, Williams and Reuser suggest the treatment of infantile Pompe's disease by administering human acid α-glucosidase to patients in need thereof. Note specifically that, although the symptoms of the disease were not alleviated in the treatment regimens of de Barsy and Williams, each of those references demonstrates a therapeutic effect, demonstrated as an increase in enzyme activity in the tissues of infant patients after administration of the enzyme (e.g., de Barsy at page 186, left column; Williams at page 420, second paragraph). Note further Reuser's disclosure of the uptake of active enzymes in fibroblasts from Pompe patients (column 16, lines 37-65). Note still further that Williams' patient was 13 months old at the start of the treatment regimen (page 418), thereby providing an expectation that the claimed treatment regimes, which use greater enzyme amounts, would have resulted in a patient survival of over one year of age.

DeBarsy, Williams and Reuser differ from the claims in that the dosage amounts disclosed therein are smaller than those recited in various embodiments recited in applicant's claims, and that the dosages are not gradually increased as recited in some other embodiments in the claims.

However, de Barsy notes that the lack of significant clinical effects was likely due to the small amount of enzyme administered owing to lack of availability, and that the efforts disclosed therein must be considered preliminary. *See* p. 189, col. 1. Thus, de

Barsy clearly suggests that increased dosage would be desirable in treating the disease. Moreover, each of Reuser (claims 18-20), Bijvoet (abstract at page 94, disclosing *in vitro* internalization of enzyme) and Van Hove (sentence spanning pages 613 and 614, disclosing endocytosis of 110 kD form of the enzyme and delivery to liver and heart upon injection) clearly suggest that relatively large amounts of the enzyme are obtained by the methods disclosed therein, and that the enzymes prepared therein are suitably targeted to the desired tissues, including muscle.

Thus, the artisan of ordinary skill, recognizing from de Barsy that high dosages would have been reasonably expected to improve the results disclosed therein, would have been motivated to have increased the enzyme dosage to the amounts recited in applicant's claims, suitable quantities of the enzymes being made available by the techniques disclosed in the Reuser, Bijvoet and Van Hove disclosures.
Moreover, the determination of a suitable dosage regimen, including the gradually increasing dosage regimen recited in the claims, clearly would have been a matter of routine optimization on the part of the artisan of ordinary skill, the determination of suitable treatment regimens being routinely determined in the pharmaceutical arts. Thus, absent some demonstration of an unexpected result, the claims must be considered obvious. In this regard note that the clinical trials described in the specification at pages 37-39 do not appear to present any significant data in that no clear results are presented. Therefore, it is respectfully submitted that no unexpected results are contained herein.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leon Lankford whose telephone number is 571-272-0917. The examiner can normally be reached on Mon-Thu 7:30-6.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Leon B Lankford Jr
Primary Examiner
Art Unit 1651